liquid-ordered and liquid-disordered coexistence region in DSPC/DOPC/POPC/Chol mixtures. By controlling lipid composition, we see distinct types of modulated liquid-liquid phase morphologies, including linear, irregular, and angular features in GUVs. These studies show that both the size and morphology of membrane rafts can be controlled by adjusting the composition and the type of low-melting lipid in mixtures with high-melting lipid and cholesterol.

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Particulate Material Effects on Pulmonary Surfactant Models

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Introduction

Pulmonary Surfactants (PS) are present in the air-liquid interface of lung alveoli. Its main function is to enhance the alveoli dilatational properties by lowering the surface tension of the system, as well as to prevent the collapse during the respiration process[1]. Particulate Material (PM) are exogenous particles which are related to some respiratory problems[2]. In the present work is reported the effects of those particles in system models of PS.

Methodology

Dipalmitoylphosphatidylcholine (DPPC) is the major component of PS and Cholesterol (Chol) is the most abundant neutral lipid. DPPC monolayers are used as models and the effects of PM and Chol were evaluated by using Oscillating Drop System (ODS) and Atomic Force Microscopy (AFM) techniques.

Results

Chol brought the Dilatational Elastic Modulus (E) to higher values evidencing an increase in the rigidity of the monolayers. Such effect is explained by the fact that Chol molecules act as space fillers turning the monolayers into more rigid structures. PM showed two different effects. The first one being the decrease of E at low PM concentration. The second one is the increase in E values which is believed to be a result of the adsorption of the particles to the monolayers.

Conclusions

PM and Chol were observed to provoke changes in some physicochemical properties of DPPC monolayers. PM as exogenous structures may cause problems to the regular functions of the PS as already reported.

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Vesicles and Phase Dynamics: Cross-Linking Effects

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We study lipid phase behavior using giant unilamellar vesicles to model cell membrane dynamics. In our system, we investigate the effects of cross-linking in the head groups position via biotinylated lipids, avidin, and its analogues. Cross-linking is the linking of two molecules (biotinylated lipids) via a cross-linking agent (avidin). Vesicles allow us to isolate the lipid rearrangement due to cross-linking, a common activity on cell surfaces. By comparing specific binding strength of the coupling and self-adhesion, we study the role that cross-linking plays in membrane behavior. Confocal microscopy gives us the ability to visualize the membrane dynamics. Using phase specific dyes, we study the changes that occur with the addition of a cross-linker to the system. Förster Resonance Energy Transfer (FRET) enables us to detect clustering on the submicron scale, beyond the limits of conventional microscopy. Using FRET we detect lipid rearrangement associated with the transition from one-phase vesicles to two-phase vesicles using two different fluorescent dyes, a donor and acceptor. Both techniques allow us to quantify the phase behavior due presence of the cross-linking agent. From this simple cross-linking system, we model membrane responses to protein complex formation and oligomerization.

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Reconstitution of Acyl Specific Phospholipid Remodeling by Purified Tafazzin In Vitro

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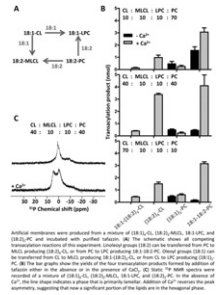
Cardiolipin is a mitochondrial phospholipid with a unique composition and distribution of acyl groups. The cardiolipin composition depends on tafazzin, a phospholipid-lysophospholipid transacylase, although the enzyme itself lacks acyl specificity. We incubated isolated tafazzin with various mixtures of phospholipids and lysophospholipids, characterized the lipid phase state by ^{31}P-NMR, and measured newly formed molecular species by mass spectrometry. Significant transacylation activity was observed only in non-bilayer lipid aggregates, in which lipids had a low packing order. The lipid phase state profoundly affected the substrate specificity of the tafazzin reaction. In particular, tetralinoleoyl-cardiolipin, a prototype molecular species, formed only under conditions that favor the inverted hexagonal phase. In isolated mitochondria, less than 2 percent of lipids participated in transacylations, suggesting that tafazzin acts only on privileged lipid domains. We propose that tafazzin reacts with non-bilayer lipids in mitochondria and that acyl specificity arises from spontaneous self-organization of these domains.



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Simulating Pores in Saturated Phosphatidylcholine Lipid Bilayers

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Lipid bilayers form the basic structure of cellular membranes. There is a large degree of diversity in the structure and composition of biological membranes. While one of the most important functions of membranes is to prohibit polar molecules from crossing the membrane, pore formation is crucial in a number of biological processes. We have used atomistic simulations to investigate the thermodynamics and kinetics of pore formation and dissipation in three saturated phosphatidylcholine bilayers, DLPC, DMPC, and DPPC. Pore formation has a large free energy cost, which increases as the tails length increases: 16 kJ/mol (DLPC), 40 kJ/mol (DMPC), and 80 kJ/mol (DPPC). We find that pore formation has a large unfavorable entropic contribution, possibly due to the constriction of water within the pore. The large unfavorable entropic contribution is compensated by a favorable enthalpic contribution to pore formation. Once formed, pores in the shorter lipid bilayers are larger and more stable than pores in bilayers with longer lipids. These results have broad implications on biological processes involving pore formation, such as lipid flip-flop, antimicrobial peptides, and cell penetrating peptides.

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Fluorinated Surfactants for Structural Studies of Membrane Proteins

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Membrane proteins are difficult to study in vitro. This is in particular related to their limited stability and motivates the search of new surfactants (e.g. 1-4), and among them, fluorinated and hemifluorinated (HFSs) surfactants. HFSs with a polymeric hydrophilic head proved to be particularly mild towards MPs (1). Surfactants were designed with chemically defined polar heads for structural applications. Lactobionamide derivative was found to be efficient in keeping several MPs water soluble and active. But it formed elongated rods (2). A new class of surfactants, the Glu- family, was synthesized, characterized in by neutron scattering (SANS) and analytical ultracentrifugation, and for its biochemical interest. The formation of rods is related to the low volumetric ratio between the polar head and hydrophobic tail. The surfactant bearing two Glucose moieties is the most promising one, leading to both homogeneous and stable complexes for both BR and the b6f. It was also shown be of particular interest for the structural investigation of membrane proteins using SANS (3).

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Nanoscale Imaging of the Piezoelectric Effect of Bilayer Phospholipid Molecules of Cell Membrane using Piezoresponse Force Microscopy*

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The dynamic piezoelectric effect of the plasma membrane and the nuclear envelope of rat A7r5 aorta smooth muscle cell is imaged with sub-3 nm spatial resolution using Piezoresponse Force Microscopy (PFM). The results verify that cell membrane is piezoelectrically active due to ordered arrangement of polar phospholipid molecules in the liquid crystalline state. A detailed analysis of the PFM signals with a 10 V / 0 V / −10 V DC bias voltage and a 10 V AC